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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,325	08/31/2001	Everett C. Pesci	UIZ-068CP	1369

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EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
1625	15

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/945,325	PESCI ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-42 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-42 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1, 3-42, 46-48 are pending. Claims 2, 43-45, 49-64 have been canceled according to the amendment filed on 1-9-2003,

Duplicate Claims

2. Applicant is advised that should claim 1 or 19 be found allowable, claims 20-34 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof since the use recited in claims 20-28 does not further limit the compound of claim 1 or 19. Should claim 1 be found allowable, claims 29-34 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof since the use recited in claims 29-34 does not further limit the compound of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the response filed on 1-9-2003, Applicant states that this issue will be address upon the allowance of claim 1 and 19.

Claim Rejections - 35 USC § 112

3. The scope rejection under 35 U.S.C. 112, first paragraph is maintained for reasons of record. The specification is only enabling for making and using 2-heptyl-3-hydroxy-4-quinolinone.

Applicant maintains that it is not necessary to provide written description for what is known by the skilled artisan, and the substituted quinoline compound is well known in art, as described in Guilhon et al. and Dekker et al. The specification therefore has provided enabling disclosure to make and use the invention as claimed.

However, the substituents in the compound of Guilhon or Dekker are unsubsituted alkyl or alkenyl, whereas the instant heptyl may have up to 15 different substituents. A quinoline compound having a heptyl further substituted with multiple substituents is unobvious over the

prior art of record, the corresponding starting materials and the process of making are not readily apparent to one of ordinary skill in the art. While the number of working examples is not controlling, the scope of the claims must be commensurate with that of the objective enablement. In the instant case, the instantly claimed compound, other than 2-heptyl-3-hydroxy-4-quinolone, has not been described. A general procedure for making these unobivous compound has not been provided in the specification. Starting materials and procedures for making the instant compound other than 2-heptyl-3-hydroxy-4-quinolone (especially those compounds wherein R10-R24 are other than hydrogen, and wherein R2-4 are all halogen) are not seen in the specification but are required. Sources are particularly pertinent because absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210 USPQ 689.

Applicant argues that the unpredictability in Bycroft's homoserine lactone compounds is not applicable to the instant quinolone compound.

However, the high degree of unpredictability is well-recognized in the pharmaceutical art, including the autoinducer art. It is well known that a small change in the structure of the compound would drastically change its biological activity. Therefore one of ordinary skill in the art would have no basis to extrapolate the result of one compound to series of compounds structurally removed therefrom. Bycroft's homoserine lactone compounds are cited to illustrate this point because at the time of the invention, quionlone compounds as autoinducers have not been described. Indeed, 2-heptyl-3-hydroxy-4-quinolone as a cell-to-cell signaling molecule (PQS) has only been identified a few years ago.

Applicant maintains that the office action is contradictory in stating that 2-heptyl-3-hydroxy-4-quinolone as a cell-to-cell signaling molecule (PQS) has only been identified a few years ago and also citing the body of homoserine lactone autoinducer art that has developed more than 10 years ago.

On the contrary, there is no contradiction. While the homoserine lactone autoinducer has been known for more than 10 years, the PQS as an autoinducer is only recently known. Furthermoe, at the time of the invention, the homoserine lactone autoinducer of Bycroft would be less than 10 years old.

Applicant argues that the two inactive analogs of 2-heptyl-3-hydroxy-4-quinolone compounds do not demonstrate the general unpredictability of the art.

The specification expressly discloses that structurally similar analogs of 2-heptyl-3-hydroxy-4-quinolone do not to activate las B'-lacZ. Indeed, there is no basis to extrapolate the results of 2-heptyl-3-hydroxy-4-quinolone to compounds embraced by the claims which are structurally further removed therefrom, since within the structurally similar quinolone compounds, as with the two inactive analogs, there exists a high degree of unpredictability.

Applicant argues that the PQS bioassay has been described, and the activity therefore can be determined easily by one of ordinary skill in the art without undue experimentation. Since Las R and/or the Rh1R proteins have been described in the background section of the specification, it would be clear to one of ordinary skill in the art would know how to determine the modulators of these proteins.

However, the opposite enhancer and inhibitor are embraced by 'modulator'. In the absence of any specific teachings in the specification on which inventive compound enhances and which inhibits, or both, undue experimentation is required. Although a working example is not required for enablement as applicant contends, some experimentation is permitted and every claimed embodiment need not be shown to possess the asserted activity, there should be a showing commensurate in scope with the claims. As stated in In re Cavallito 127, USPQ 202, " where the applicant seeks to obtain a monopoly in exchange for his disclosure of a group of compounds, there should be a disclosure which gives reasonable assurance that all, or substantially all of them are useful....an applicant is not entitled to a claim for a group of compounds merely on the basis of a showing that a selected few are useful and a general suggestion of a similar utility in the others". In the instant case, an example for a compound that 'modulates' the activity of PQS, either enhances or inhibits the antoinducer activity of PQS, 'modulates' or antagonize the activity of Las R and/or the Rh1R proteins as recited in the instant claims 29-34 has not been described in the specification. Since the only compound shown is 2-heptyl-3-hydroxy-4-quinolinone (PQS), and no specific compounds that inhibit or enhance PQS are described, undue experimentation would be required for one of ordinary skill in the art to use these compounds as claimed. Furthermore, in the instant autoinducer art, where there is a high

degree of unpredictability exists, the required disclosure will be greater than for the disclosure of an invention involving a predictable factor such as a mechanical or electrical element. In re Vaeck, 20 USPQ 2d 1438, especially when PQS is in its infancy stage.

In conclusion, in view of the state of the art, the high degree of unpredictability of the art, the absence of specific working examples, the scope of the claims does not commensurate with that of the objective enablement. Sufficient teaching and guidance have not been provided in the specification to enable one of ordinary skill in the art to practice the invention as claimed without undue experimentation.

Claim Rejections - 35 USC § 102

4. The rejection for Claims 1, 4, 10-14, 19-28, 32-42, 46-48 under 35 U.S.C. 102(b) as being anticipated by Takeda (Hakko Kogaku Zasshi (1959), 37, 59-63, abstract) is maintained for reasons of record.

Applicant asserts that Takeda does not isolate 2-heptyl-3-hydroxy-4-quinolone (PQS), citing that Takeda used only melting point and ultraviolet absorption spectrum to identify the compound whereas applicant identified the 2-heptyl-3-hydroxy-4-quinolone by more sophisticated methods. On the contrary, the prior art compound, 2-heptyl-3-hydroxy-4-quinolone is identical to the instant compound. Furthermore, it is also isolated from the culture of *pseudomonas aeruginosa* as in the instant. Takeda's compound expressly anticipates the claimed invention. The use of different techniques to identify the same compound is irrelevant absent the showing that the method employed by Takeda does not lead to 2-heptyl-3-hydroxy-4-quinolone.

Applicant further maintains that PQS does not have detectable anti-*staphylococcus aureus* or anti-*E. coli* activity whereas Takeda finds the compound to have antibacterial action on gram-positive bacteria. However, Takeda teaches that the compound has only ***weak*** antibacterial action on gram-positive bacteria. Depending on the experimental conditions and the purity of the compound, the same compound may exhibit weak or un-detectable activity. This is no indication that Takeda's compound is not 2-heptyl-3-hydroxy-4-quinolone as asserted by applicant.

When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP § 716.07. Applicant has provided arguments, but not convincing facts rebutting the presumption of operability.

Claim Rejections - 35 USC § 112

5. The rejection for Claims 9, 10 under 35 U.S.C. 112, second paragraph is withdrawn because the amendment has obviated the rejection.

Specification/ Drawings

6. The specification is objected to because the figures in the specification do not come within the purview of 37 CFR 1.58(a), which permits only tables, chemical and mathematical formulas in the specification in lieu of formal drawings.

Formal drawings in accordance to 37 C.F.R. 1.81, 1.83-1.85 are required. See MPEP 608.01 and 608.02.

A brief description of the drawings is not found in the specification but is required.

In the response filed on 1-9-2003, Applicant states that this issue will be address upon the allowance of the claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 14, Q has no antecedent basis in the base claim 1. The rejection is applicable to claims 15, 16, which are dependent on claim 14.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Evelyn Huang
Primary Examiner
Art Unit 1625

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